Task-Specific Fixation Behavior in Macular Disease

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PURPOSE. Persons with central scotomas frequently use a preferred retinal locus (PRL) in place of the damaged fovea to fixate a target. Here the authors use a novel statistical technique to determine whether the retinal locus used for fixating a point target is the same as that used for reading words.

METHODS. Nine subjects with established macular disease and bilateral central scotomas were recruited. The retinal area used for fixating a point target and words of text was measured using a microperimeter. A nonparametric spatial statistical technique was used to identify whether fixation points were the same for each of these two tasks.

RESULTS. The spatial distribution of fixation points was different for point fixation and word reading in all subjects with macular disease ($P < 0.01$). Fixation stability was also poorer for the word reading task than the fixation task ($P < 0.05$). For control subjects without macular disease, the distribution of fixation was the same for each task ($P > 0.5$).

CONCLUSIONS. Fixation behavior in persons with macular disease is not the same for fixating a point target and for fixating words in a reading task. It cannot be assumed that measuring a patient’s fixation to a discrete point target accurately simulates their fixation performance on other tasks. (Invest Ophthalmol Vis Sci. 2011;52:411–416) DOI:10.1167/iovs.10-5473

Persons with central scotomas caused by macular disease are not able to see an object if it is viewed with the fovea. To observe a target, it is necessary for them to make an eye movement and to use the peripheral retina in place of the damaged fovea.3 Most persons with macular disease use a specific retinal area for this task, known as the preferred retinal locus (PRL).2,4 For persons with good vision who are forced by an experimentally induced artificial scotoma to use the peripheral retina, reading is most efficient when the text is fixated with the retina superior to the fovea, that is, by making an eye movement upward and moving the fovea above the word of interest in the visual field space.8 However, this finding has not been replicated in persons with macular disease. In a large study of 825 patients, Fletcher and Schuchard4 did not find any significant differences in reading speed based on the location of the PRL. More recent research has also failed to find a relationship between fixation position and reading speed.5,7

A possible explanation for the lack of relationship between PRL position and reading speed in patients with macular disease is that the PRL is not often assessed during a reading task. Generally, it is assessed by asking the patient to look toward a point target.5 However, it is known that changing the fixation target can cause different regions of the retina to be used, such as when viewing a dim target rather than a bright target.9 It has also been shown that multiple PRLs can be elicited during complex tasks such as reading.10

Studies that have measured fixation position during reading give equivocal results. In an early study, Timberlake et al.11 found that the same retinal area is used for reading scrolled text and for fixating a point target, although they also recently identified some patients who use different retinal loci for reading text and fixating a target.6 Some authors report the use of multiple PRLs when reading a single word, such as using a larger PRL with poorer resolution to observe word shape and position and a smaller locus with better resolution to identify characters within the word.10

To assess accurately the retinal area used for fixating a target, a device is required that simultaneously presents stimuli and images the retina. Although a direct ophthalmoscope or fundus camera can be used for this task, most research in this area has used a confocal scanning laser ophthalmoscope (cSLO) equipped with a visible helium-neon laser such as the Rodenstock cSLO (SLO-101; Rodenstock Instruments, Düsseldorf, Germany) (Fletcher DC, et al. JOVS 1993;349:ARVO Abstract “787”). The HeNe laser in the cSLO can create very bright stimuli, but this Rodenstock cSLO is limited to producing only monochromatic red targets, the image can suffer from visible raster artifacts, and the retinal image produced has some raster distortion.13 Although other scanning laser ophthalmoscopes do not have these limitations, the Rodenstock cSLO has been used most commonly for published work examining fixation behavior in vision rehabilitation research.

The microperimeter (MP-1; Nidek Technologies, Padova, Italy) is a clinical instrument that can display dynamic stimuli on an LCD display while simultaneously imaging the retina using an infrared camera. Unlike the Rodenstock cSLO, this instrument can display full-color stimuli that more accurately simulate reading at contrast and luminance levels more similar to those of conventional reading. The text presented is black on a white background, at approximately equivalent luminance to that of reading a hardcover book under good lighting, simulating the glare and intraocular scatter experienced by patients performing a real reading task.

In this article we describe a technique to enable this instrument to be used for fixation analyses while persons performed more complex tasks such as fixating words. We compared the locus of fixation used when fixating a point target and when fixating words for a group of subjects with macular disease. We then applied a novel statistical test to compare the parameters of fixation for these two tasks. Although word fixation is not the same as reading continuous text, we believe that investi-
gating fixation while observing words can aid our understanding of the reading process.

**METHODS**

**Participants and Ethical Approval**

Nine persons with central scotomas were recruited from the low-vision and medical retina clinics at Moorfields Eye Hospital in London (Table 1). All subjects had at least a 1-year history of bilateral central visual loss and had attended a low vision clinic to ensure the optimal spectacle correction and low vision aids were dispensed.

The study was approved by the Moorfields and Whittington Research Ethics committees and conformed to the Declaration of Helsinki. Subjects gave their informed consent before data collection.

**Stimulus Display System and Calibration**

All stimuli were presented on the internal display of the microperimeter (MP-1; Nidek), which consists of an LCD display for stimulus presentation, an infrared video retinal camera to monitor eye position, and a color fundus camera for capturing a still retinal image. The optics of the MP-1 allow an “almost” Maxwellian view.15 Stimuli were generated on a supplementary laptop computer (MacBook Pro; Apple, Cupertino, CA) running computational software (MatLab; Mathworks, Natick, MA) and elements of the Psychophysics toolbox.16 The video output of this laptop was connected to the VGA input on the side of the microperimeter. A switch box allowed the video input to be changed between the laptop and the microperimeter control computer. This technique allows the eye tracking and retinal imaging capabilities of the microperimeter to be used while any image (or video) created on the laptop is shown on the microperimeter display.

We have previously described a method for calculating the parameters of the microperimeter screen and presenting stimuli on the screen using a supplementary computer (Crossland MD, et al. IOVS 2009;50:ARVO E-Abstract 4735). Briefly, the center of the microperimeter internal display screen was found by interpolating the center of a circle that encompasses all the pixels visible on the display when looking into the microperimeter. After this, the relationship between pixel position on the internal display and eye position (in degrees) was calculated by measuring the eye position, using the eye tracking facility of the microperimeter, while five control subjects observed targets created by the supplementary computer presented at specified locations on the internal display. Finally, eye position was measured and a retinal image was captured (using the onboard fundus camera of the microperimeter) while the subjects observed the same targets to determine the retinal coordinates of the eye position data recorded by the eye tracker. This analysis has shown, for our microperimeter, that the screen center is at pixel position (367,249), that each pixel of target decentration leads to a 0.085° movement to be recorded in the fixation file (95% CI, 0.081°-0.088°), and that each pixel of target decentration causes a 2.37° movement on the image file (95% CI, 2.32-2.62 pixels). There were no significant differences in these values between five observers (P > 0.5 in all cases). Knowledge of these parameters makes it straightforward to relate fixation position (from the microperimeter fixation data file) to fixation position on the retinal image captured on the microperimeter.

The luminance of the internal display was measured at the exit pupil of the instrument using a photometer supplied by Nidek and was 126 cd/m² at maximum brightness.

**Point Fixation Task**

The fixation target used was a black circle of 1° diameter with a central white detail of 0.3° diameter, displayed against a full white background of 126 cd/m². Subjects were asked to look at the center of the fixation target so that it was as clear as possible. Once the subject reported being able to see the target clearly, they were asked to hold the eye still for a period of 30 seconds, during which eye position was recorded.

**Word Fixation Task**

Four-word sentences were constructed using a random sentence generator we have previously described.17 Each sentence was presented, one word at a time, centered at the middle of the display, using a rapid serial visual presentation technique (RSVP).18 Words were presented in black Courier font, against a white background, with a height of three times visual acuity. Subjects were asked to read each word of every sentence silently. Reading speed was altered for each sentence by manipulating word presentation duration using the psychophysical method of constant stimuli. Each subject read four sentences at each of eight word-presentation durations. These exposure durations were 0.083, 0.13, 0.2, 0.32, 0.5, 1, 2, and 4 seconds, corresponding to a reading speed of 720 to 15 words/min. Not all subjects were able to read words at the fastest exposure duration, but all could read comfortably at the slowest reading speed. Threshold reading speed was, therefore, between the slowest and the fastest exposure duration. Multiple eye position files of 30 seconds’ duration were recorded during the word-fixation task.

**Procedure**

The eye with better visual acuity was assessed for all subjects, with the dominant eye used if visual acuity was equal. The contralateral eye was occluded in all instances. Subjects were asked to fixate the standard fixation cross (generated with the supplied microperimeter software), and eye position was measured. After this, eye position was measured as the subject viewed the same stimulus produced by the supplementary computer to determine any offset in display position between stimuli presented with each computer. Each subject performed the point-fixation and the word-fixation task once, in counterbalanced order. Finally, a retinal photograph was taken.

**Statistical Analysis**

Eye position data files were analyzed retrospectively. Eye position was converted to retinal coordinates, and the retinal location corresponding to the center of the fixation target for each recorded fixation was plotted on the retinal image (Fig. 1). Fixation stability was recorded for each trial by measuring the area of an ellipse that encompasses 68% of fixation positions (bivariate contour ellipse area [BCEA]).19

An analysis adopted from spatial statistics was used to assess whether subjects used the same regions of the retina for fixating points and fixating words. The data arising from this experiment are a random variable from a spatial point process; therefore, an appropriate method from the catalog of methods for analyzing spatial statistics is required. In this analysis, the fixations recorded in two-dimensional space are assumed to be values generated from a multivariate spatial point process, with each point being 1 of 2 qualitatively distinguishable types. Spatial segregation is assumed to occur if, within some area, particular types of points predominate rather than being randomly

<table>
<thead>
<tr>
<th>Table 1. Demographic and Clinical Data for Each Subject</th>
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<tr>
<td>Subject</td>
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<td>M1</td>
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<td>M2</td>
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<td>M3</td>
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<td>M4</td>
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<td>M5</td>
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<tr>
<td>M6</td>
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<td>M7</td>
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<tr>
<td>M8</td>
</tr>
<tr>
<td>M9</td>
</tr>
<tr>
<td>C1</td>
</tr>
<tr>
<td>C2</td>
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AMD, age-related macular disease; CSC, central serous chorioretinopathy.
intermingled. A technique modified from Diggle et al.\textsuperscript{20} and implemented in the spatialkernel and splancs packages (Barry Rowlingson, Peter Diggle, adapted, packaged for R by Roger Bivand, pxp functions by Giovanni Petris, and goodness of fit by Stephen Eglen. Splancs: spatial and space-time point pattern analysis, R package version 2.01-24. \url{http://www.maths.lancs.ac.uk/~rowlings/Splancs/}) using the open-source statistical programming environment R\textsuperscript{21–23} was used to assess this segregation of the fixation points. The purpose-written R script is given as Supplementary Material, \url{http://www.iovs.org/lookup/suppl/doi:10.1167/iovs.10-5473/-/DCSupplemental}, and is illustrated using data from the two control subjects and two patients. In short, this method gives a probability value against the null hypothesis that the fixation coordinates from the different tasks are yielded from the same spatial point process and are, therefore, not segregated. Some modifications from the original method were made. First, several fixations fall on exactly the same location (with the same coordinates) because of the measurement precision of the instrumentation. Moreover, the technique is very sensitive to small levels of segregation especially when the sample size is large, as in the case with these data. To overcome these limitations, random Gaussian noise was first added to every recorded \((x,y)\) fixation for both controls and patients. This also has the effect of randomly “mixing” the two spatial processes further. For the purpose of this analysis, it is assumed that if a statistically significant effect remains after this mixing, it provides clear evidence that the fixations for each task are indeed generated from a different spatial process. The method uses a Monte-Carlo technique to derive probability values against the null hypothesis.

**RESULTS**

**Fixation Position**

Segregation analysis indicated that there was overwhelming evidence for the subjects with macular disease using different regions of retina for each task. For 8 of the 9 subjects with macular disease, the segregation analysis returned \(P = 0.001\) against the null hypothesis that the regions were coincident (not segregated). For one subject (M5), the segregation analysis returned a slightly higher probability value (0.008), but this still represents considerable statistical evidence. The \(P\) values were estimated from 1000 Monte-Carlo trials. Figure 1 shows the fixation positions superimposed onto the retinal image for all the subjects with macular disease.

For comparison, data for two control subjects are shown in Figure 2. Data for control subjects were collected under identical conditions except that words were not presented at exposure durations of 1, 2, and 4 seconds. Instead, exposures of 0.016, 0.033, and 0.05 seconds were added such that subjects observed words corresponding to a reading speed of 3750 to 120 words/min. It can be seen that the fixation position for both tasks was the same as and coincident with the foveal center in the observers without eye disease. Segregation analysis supported this visual impression with no evidence that the fixations for each task come from different spatial processes in these subjects (\(P = 0.76\) for control subject C1; \(P = 0.34\) for control subject C2).

Table 2 shows the distance between the center of the fixation locus for each task for every subject. The mean sepa-
ration of the center of each locus was 2.8° for those with macular disease and 0.2° for the control subjects.

**Fixation Stability**

Fixation was less stable for the word fixation task than for the point fixation task, with a mean BCEA for point fixation of 6078 minarc² and a mean BCEA for word fixation of 16,300 minarc² (matched pairs; \( P < 0.05 \)). Table 2 shows fixation stability data for all subjects.

**DISCUSSION**

In this sample each of the nine subjects with macular disease used a different retinal region for point fixation and for word fixation. This indicates that for persons with macular disease, it cannot be assumed that the PRL used for fixating a point target is necessarily the same as the retinal point used for any other task.

We used a novel application of a statistical test to analyze eye position files. This procedure is nonparametric and makes no assumption about the underlying shape of the distributions generated by the point process, which is appropriate because many authors have shown that fixation data are rarely normally distributed.\(^{19,24} \) This test appears to be sensitive to small changes between distributions, but the fact that our control subjects were shown to use the same retinal area for word fixation and point fixation with this technique indicated that the differences found in our patient data were unlikely to have been caused by type 1 error. The technique presented here may have other applications for examining spatial distributions of fixation points, and we believe we asked subjects not to make intra-word saccades and fixations as part of their reading strategy.

For other subjects, such as M8 and M9, if the retinal area for point fixation were used for reading, the entire word would fall into relatively healthier retina. We speculate that the reason the distribution was different for the two tasks is a consequence of a reduced visual span: that is, if the visual span is smaller than the word length, an additional eye movement is needed to read an entire word. This extra fixation would lead to a different fixation distribution for word reading. In persons with macular disease, visual span is approximately halved.\(^{25} \) Although the mean word length of our sentences was only 3.5 letters, some words were considerably longer (e.g., leading [seven letters]). Although a seven-letter word is likely to fall within the visual span of someone with good vision,\(^{26} \) at least one eye movement would be required if the visual span was beneath this value. This is the likely reason for the greater horizontal extent of the fixation pattern for word fixation in subjects M1, M7, and M8. Unfortunately, we did not measure visual span in our subjects.

Some subjects, such as M5 and M6, showed retinal fixation loci centered at similar points with different distributions. In each case, fixation was more stable for the point target than for the word. Our statistical technique shows that these distributions were significantly different for the two tasks.

Although the fixation location was statistically different in those subjects who used a different retinal area for each task, Figure 1 shows that none moved fixation into different quadrants of retina. Therefore, our results do not wholly explain the poor relationship between PRL position and reading speed found in previous studies. This is likely to be attributed to the fact that RSVP is not an accurate simulation of reading continuous text. We used RSVP text presentation to reduce the effect of eye movements and to minimize the difficulties of determining which retinal position is attending to a given portion of continuous text at any given time.

In previous control studies, we attempted to use the reverse correlation technique of Timberlake et al.\(^{9} \) on this instrument without success. It is tempting to speculate that if the PRL were measured for continuous text, a third PRL would have been identified that might have been in a different quadrant of retina.

A potential confounding factor is that the words we presented were centered at the same point as the fixation target. It is known that the “landing position” of eye movements when reading continuous text is between the start and the center of the word.\(^{27} \) If our subjects were indeed

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**Table 2. Separation of the Centers of the Mean Fixation Position for Fixation and Reading and Fixation Stability Values for Each Task**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Distance between Fixation and Reading PRL (°)</th>
<th>BCEA for Fixation (minarc²)</th>
<th>BCEA for Reading (minarc²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>2.8</td>
<td>152</td>
<td>7820</td>
</tr>
<tr>
<td>M2</td>
<td>2.8</td>
<td>26200</td>
<td>39300</td>
</tr>
<tr>
<td>M3</td>
<td>7.7</td>
<td>1850</td>
<td>9210</td>
</tr>
<tr>
<td>M4</td>
<td>3.3</td>
<td>8800</td>
<td>14900</td>
</tr>
<tr>
<td>M5</td>
<td>0.70</td>
<td>9967</td>
<td>6160</td>
</tr>
<tr>
<td>M6</td>
<td>0.21</td>
<td>775</td>
<td>36800</td>
</tr>
<tr>
<td>M7</td>
<td>4.4</td>
<td>1780</td>
<td>3320</td>
</tr>
<tr>
<td>M8</td>
<td>2.2</td>
<td>844</td>
<td>16000</td>
</tr>
<tr>
<td>M9</td>
<td>1.3</td>
<td>4100</td>
<td>13000</td>
</tr>
<tr>
<td>C1</td>
<td>0.21</td>
<td>88</td>
<td>126</td>
</tr>
<tr>
<td>C2</td>
<td>0.20</td>
<td>87</td>
<td>447</td>
</tr>
<tr>
<td>C1 (reading 5° letters)</td>
<td>0.21</td>
<td>362</td>
<td>1850</td>
</tr>
<tr>
<td>C2 (reading 5° letters)</td>
<td>0.08</td>
<td>195</td>
<td>472</td>
</tr>
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observing to the left of the center of the word, the word center would have fallen to the right (in visual field) of the fixation point. On Figure 1 this would be seen as the green dots appearing to the right of the black dots. This effect is only seen for subjects M1, M3, and M7, so it was clearly not a strategy for all our patients.

A reviewer of this manuscript commented that although none of our control subjects exhibited this performance, the letters might have been too small for this effect to have been observed. Another experiment was performed in which our control subjects observed words presented at x-height of 5° so that differences in fixation distributions would be more apparent: the distance of a one-letter shift would approximately match the diameter of the optic nerve head. The subjects were naive to the purpose of this additional experiment, and the instructions were identical to those given the patients. Neither control subject was an author of the paper (one was a doctoral candidate in a different laboratory and the other was a departmental administrator). Results of this experiment are shown in Figure 3. It can be seen that there was no systematic shift in fixation position when observing larger text. This finding was confirmed statistically (P = 0.19 for C1; P = 0.48 for C2). If the magnitude of the offset between fixation positions was indeed related to the size of the letters, we would expect this offset to be correlated to visual acuity (because this is related to target size). This was not the case. Linear regression did not show a significant correlation between visual acuity and distance between the PRLs (r² = 0.086; P = 0.38).

Another problem with our experimental design was that some of the word exposure durations were much longer than those needed to identify the word and that eye movements could be made in this time. Data were collected across several trials rather than simply when words were presented at or near threshold reading speed. This is a likely explanation for the poorer fixation stability in our control subjects when they observed the words rather than when they fixated the point target. Our control subjects were not age matched to our subjects with macular disease, but it is known that fixation stability does not deteriorate with age.28,29

We believe this is the first time the microperimeter has been used with a supplementary computer to generate stimuli while fixation position is recorded. A particular strength of this system is that the retina can be viewed while dynamic, full-color images of luminance similar to printed text are displayed. The possibility that this instrument can be used for observing retinal location in persons with macular disease during such tasks as watching a film is exciting, and we encourage other researchers in the field to use this instrument modification in their studies.

In conclusion, we have shown that fixation distribution is not the same when fixating a word as it is when fixating a point target. This indicates that PRL position cannot be defined solely by asking a patient to observe a point target or a fixation cross. Rather, the PRL should be examined separately for each task because it is likely to be different for each task.

Acknowledgments
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References

FIGURE 3. Retinal coordinates of the center of each fixation target for two control subjects, when text was much larger (x-height 5°). Green crosses: retinal position of center of word. Black crosses: retinal position of center of fixation cross. Note that the fixation point and word fixation point are still coincident and at the foveal center.


